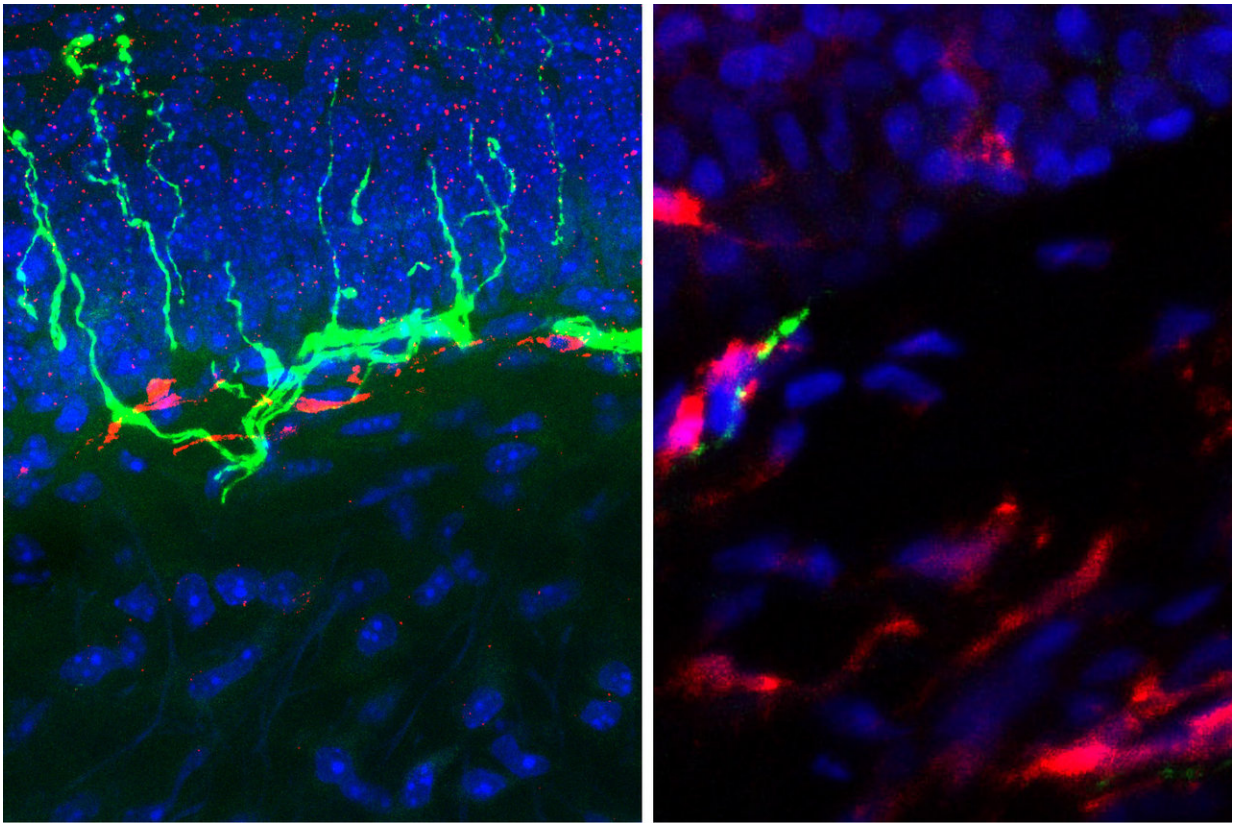


Non-opioid drug relieves pain in mice, targets immune cells

July 5 2018



In skin biopsies from the legs of healthy people (left) there are abundant sensory nerve fibers (green) but few macrophages (red). Meanwhile, in biopsies from patients with pain due to diabetic neuropathy (right), macrophages (red) surround degenerating nerve fibers (green). Credit: Mohopatra lab

Faced with the epidemic of opioid addiction, researchers have been

charged with finding other strategies to treat pain. Their efforts largely have focused on nerve cells that transmit pain signals to the spinal cord and brain. But new research, led by scientists at Washington University School of Medicine in St. Louis, shows that targeting receptors on immune cells may be more effective, particularly for chronic pain.

Recently, a non-opioid, investigational drug called EMA401 has shown promise as a treatment for lingering [nerve](#) pain following shingles infection. While trying to understand how that drug helped control pain, the Washington University research team was surprised to find that it doesn't hit nerve cells; rather, it targets a receptor on immune cells.

Their findings are published July 2 in *The Journal of Neuroscience*.

"We are in dire need of good pain-killing drugs, particularly non-opioid drugs," said principal investigator D.P. Mohapatra, Ph.D., an associate professor in anesthesiology. "Generally, scientists have the understanding that targets for treating pain must be within the nervous system. It turns out that the target here is not on nerve cells, but on immune cells called macrophages."

The investigational drug inhibits the angiotensin II type 2 receptor that is targeted by medications that lower blood pressure. Angiotensin is a hormone that causes blood vessels to constrict, increasing blood pressure.

This drug was thought to work by interacting with the type 2 receptor on nerve cells—the same cells that carry [pain signals](#). But when Mohapatra and his colleagues at the Washington University Pain Center looked more closely, they found that theory was wrong.

"When we took nerve cells from mice, put them in a culture dish and added the angiotensin hormone, nothing happened," said co-investigator

Andrew Shepherd, Ph.D., an instructor in anesthesiology. "There was no angiotensin type 2 receptor on sensory neurons, so pain signals couldn't be transmitted."

But in other experiments in which they injected the angiotensin hormone into mice, the animals indicated they felt pain and withdrew their paws when touched.

"We found that the receptor the drug affected wasn't on the nerve cells; it was on macrophages, the immune cells," Shepherd said. "When we added macrophages to the dish alongside the nerve [cells](#), the angiotensin could 'talk' to the macrophages, and then the macrophages 'talked' to the [nerve cells](#), which then transmitted pain signals."

When the researchers reduced the number of macrophages in mice, the animals didn't appear to feel pain in response to an [angiotensin](#) injection. But as the macrophages repopulated over the course of a few days, the response to pain returned. To support these observations in mice and the culture dish, the researchers also have found increased numbers of macrophages alongside degenerating nerve fibers in skin biopsies taken from the legs of patients who have diabetic neuropathy.

Increasing the number of potential targets for painkillers and including targets such as [receptors](#) on [immune cells](#) may make it possible to develop more effective painkilling drugs with fewer side effects, Mohapatra said.

"The beauty of this [drug](#) is that, unlike an opioid, it doesn't cross the blood-brain barrier, so right away you eliminate a number of potentially harmful side effects, including addiction and the potential for abuse," he said. "And by widening the scope of potential targets to macrophages, it may be possible to develop more effective therapies for chronic, neuropathic [pain](#)."

More information: Shepherd AJ, et al. Angiotensin II triggers peripheral macrophage-to-sensory neuron redox crosstalk to elicit pain. *The Journal of Neuroscience*, July 2, 2018.

Provided by Washington University School of Medicine

Citation: Non-opioid drug relieves pain in mice, targets immune cells (2018, July 5) retrieved 20 April 2024 from

<https://medicalxpress.com/news/2018-07-non-opioid-drug-relieves-pain-mice.html>

This document is subject to copyright. Apart from any fair dealing for the purpose of private study or research, no part may be reproduced without the written permission. The content is provided for information purposes only.